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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/619,047 07/19/00 LENG

J CHEM1110

HM12/0727

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EXAMINER

PAK, Y

ART UNIT

PAPER NUMBER

1652

17

DATE MAILED:

07/27/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application N .

09/619,047

Applicant(s)

LENG, JAY

Examiner

Yong Pak

Art Unit

1652

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on 02 July 2001.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-65 is/are pending in the application.
- 4a) Of the above claim(s) 9-65 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3 and 6-8 is/are rejected.
- 7) ☐ Claim(s) 4-5 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s) _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

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DETAILED ACTION

The response filed on July 2, 2001 has been entered.

Claims 1-65 are pending.

Election/Restrictions

Applicant's election with traverse of Group I (claims 1-8) in Paper No. 16 is acknowledged. Additionally, applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claims 1, 3 and 6-7 are generic. *Renilla* luciferases having different recognition site cleavable by caspase-family proteases are patentably distinct species of the claimed invention. Applicants are required to elect one recognition sequence and its corresponding protease.

During a telephone conversation with Ms. Haile on July 23, 2001, a species election was made with traverse to prosecute a polypeptide comprising the recognition site, DEVD, cleavable by Caspase-3.

Claims 9-65 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Drawings

Drawings filed concurrently with the application has been objected by the Draftsman. Please refer to the attached PTO-948 form for details.

Claim Objections

The sequences in claims 3 should be identified by SEQ ID numbers and must comply with the Sequence Rules, see 37 CFR 1.821-1.825.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3 and 6-8 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1 is drawn to a modified luciferase having a recognition site cleavable by any protease and claim 2 limits the source of the modified polypeptide to *Renilla*. Since there is no limit to structure or source of the polypeptide, these claims are drawn to a genus of polypeptides of unlimited structure described by the function of having a decrease luciferase activity upon cleavage by a protease. The specification only describes SEQ ID NO:2, a luciferase from *Renilla reniformis*, substituted with a recognition site at residues 197-200 wherein cleavage by a caspase-family protease decreases luciferase activity. A description of only one type of *Renilla* luciferase modified with several recognition sites out of a diverse genus of polypeptides is not

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representative of the species that have different structures but the same function.

Therefore, the specification fails to describe other representative species by identifying characteristics or structural properties other than the functionality of being a polypeptide cleavable by a protease, wherein cleavage results in a decrease in luciferase activity.

Claims 3 and 7-8 limit the recognition site of claim 1 to a sequence cleavable by caspase-3 substituted in any region of a luciferase, wherein cleavage by caspase-3 results in a decrease in luciferase activity. Since there is no limit to structure or source of the luciferase, these claims are drawn to a genus of polypeptides described by the function of having a decrease luciferase activity upon cleavage by caspase-3. A description of only one type of *Renilla* luciferase modified with several recognition sites out of a diverse genus of polypeptides is not representative of the species that have different structures but the same function. One member of this genus is not representative of the species that have different structures but the same function. Therefore, the specification fails to describe other representative species by identifying characteristics or structural properties other than the functionality of being a polypeptide cleavable by a protease, wherein cleavage results in a decrease in luciferase activity.

Given this lack of description of the representative species encompassed by the genus of the claims, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the inventions of claims 1-3 and 6-8.

Claim Rejections - 35 USC § 102

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(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Thompson et al.

Thompson et al. teach a luciferase having a recognition site cleavable by *dmr* chymotrypsin and trypsin, wherein cleavage results in short intracellular half-life (abstract, page 18766 and Fig. 2, page 18768). Therefore, the reference of Thompson et al. anticipates claim 1.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-3 and 6-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lorenz et al. in view of Xu et al.

Lorenz et al. teach a *Renilla* luciferases (page 31, 2nd column and page 32, 2nd column) and that luciferases are efficient marker proteins in monitoring gene expression in mammalian cells (page 32, 1st column).

The difference between the reference of Lorenz et al. and the instant invention is that the reference of Lorenz et al. does not teach a *Renilla* luciferase having DEVD, the recognition and cleavage site of caspase-3.

Xu et al. teach that the recognition and cleavage site of caspase-3 is DEVD (page 2034, 3rd paragraph) and that caspase-3 is activated during cell death (page 2034, 3rd paragraph). Xu et al. teach a green fluorescent protein (GFP) linked to a blue fluorescent protein by a peptide containing the DEVD sequence can be used as a marker protein to detect caspase-3 activity during cellular apoptosis (page 2034).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to make a *Renilla* luciferase substituted with a recognition site of caspase-3, DEVD. The motivation of substituting DEVD into a luciferase, a marker protein like GFP or BFP, is to detect caspase-3 activity during apoptosis by monitoring luminescence given off by luciferase. One of ordinary skill in the art would have had a reasonable expectation of success since short peptides are successfully substituted into a polypeptide.

Claims 4-5 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong Pak whose telephone number is 703-308-9363. The examiner can normally be reached on Monday through Friday from 8:30 a.m. to 5:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy, can be reached on (703) 308-3804. The fax phone number for the organization where this application or proceeding is assigned is 703-746-3173.

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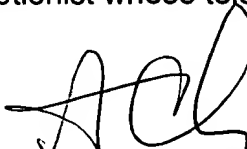
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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Yong Pak
Patent Examiner

July 25, 2001



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